ELSEVIER

The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

FEATURED ARTICLES

Comparative cost-effectiveness of the HeartWare versus HeartMate II left ventricular assist devices used in the United Kingdom National Health Service bridge-to-transplant program for patients with heart failure

Ruth Pulikottil-Jacob, MSc,[a] Gaurav Suri, MSc,[a] Martin Connock, PhD,[a] Ngianga-Bakwin Kandala, PhD,[a] Paul Sutcliffe, PhD,[a] Hendramoorthy Maheswaran, PhD,[a] Nicholas R. Banner, FRCP,[b] and Aileen Clarke, MD[a]

From the [a]Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry; and [b]Heart Failure Care Group, Royal Brompton and Harefield NHS Foundation Trust, London, and Institute of Cardiovascular Medicine and Science, National Heart and Lung Institute, Imperial College, London, and Clinical Effectiveness Unit, Royal College of Surgeons of London.

KEYWORDS:
left ventricular assist device;
heart failure;
bridge to transplant;
clinical effectiveness;
cost-effectiveness analysis;
economic model

BACKGROUND: Patients with advanced heart failure may receive a left ventricular assist device (LVAD) as part of a bridge-to-transplant (BTT) strategy. The United Kingdom National Health Service (UK NHS) has financed a BTT program in which the predominant LVADs used have been the HeartMate II (HM II; Thoratec, Pleasanton, CA) and HeartWare (HW; HeartWare International, Inc. Framingham, MA). We aimed to compare the cost-effectiveness of the use of these within the NHS program.

METHODS: Individual patient data from the UK NHS Blood and Transplant Data Base were analyzed with Kaplan-Meier and competing outcomes methodologies. Outcomes were time to death, time to heart transplant (HT), and cumulative incidences of HT, death on LVAD support, and LVAD explantation. A semi-Markov multistate economic model was built to assess cost-effectiveness. The perspective was from the NHS, discount rates were 3.5%. Outcomes were quality-adjusted life-years (QALYs) and incremental cost (2011 prices in GB£) per QALY (ICER) for HW vs HM II.

RESULTS: Survival was better with HW support than with HM II. Cumulative incidence of HT was low for both groups (11% at ~2 years). HW patients accrued 4.99 lifetime QALYs costing £258,913 ($410,970), HM II patients accrued 3.84 QALYs costing £231,871 ($368,048); deterministic and probabilistic ICERs for HW vs HM II were £23,530 ($37,349) and £20,799 ($33,014), respectively.

CONCLUSIONS: Patients In the UK BTT program who received the HW LVAD had a better clinical outcome than those who received the HM II, and the HW was more cost-effective. This result needs to be reassessed in a randomized controlled trial comparing the 2 devices.

J Heart Lung Transplant 2014;33:350–358

Reprint requests: Aileen Clarke, MD, Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, CV4 7AL, UK. Telphone: +44 0 24761 50063. Fax: +44 0 24765 28375.

E-mail address: aileen.clarke@warwick.ac.uk

1053-2498/$ - see front matter

http://dx.doi.org/10.1016/j.healun.2014.01.003

Heart transplant (HT) offers the optimal treatment for patients with advanced heart failure, improving survival and quality of life. In the United Kingdom (UK), approximately 750,000 people have heart failure, with an estimated 27,000 new cases annually.[1] Since 2000, the supply of donor hearts has diminished.[2] and use of left ventricular assist devices (LVADs) as a bridge to transplant (BTT) has been increasing.[3–5]

High demand for LVADs internationally has stimulated significant technologic advances. First-generation pulsatile LVADs were replaced by smaller second-generation continuous-flow LVADs, with improvements in reliability and reductions in adverse events.[6] These devices are costly but can maintain an individuals' cardiac function and improve survival and quality of life until a donor heart becomes available. Currently, the 2 most frequently used LVADs in the UK are the HeartMate II (HM II; Thoratec, Pleasanton, CA) and the HeartWare (HW, HeartWare International, Framingham, MA).

The HM II second-generation device is placed below the diaphragm and necessitates abdominal surgery in patients who are already at high risk because of poor cardiac function. The HW device is a smaller third-generation LVAD that is placed in the pericardial space, thus avoiding the need for abdominal surgery. The HM II has been implanted in more than 3,000 patients worldwide.[7] In 2005, it received Conformité Européenne (CE) approval, allowing for commercial sale in Europe. The HW received CE approval in 2009.[8–10]

Several studies have highlighted the benefits of these second- and third-generation LVADs, but no direct comparisons have been made between them.[11–15] Choice of LVAD may have important implications for patients and for the cost and sustainability of expenditure for an expanding candidate population; therefore, estimating the relative clinical and cost-effectiveness of these devices is important. The objectives of this study were, firstly, to investigate the clinical outcomes for those individuals implanted with HM II and HW devices in the UK, and secondly, to estimate the cost-effectiveness of the HW VAD relative to the HM II LVAD for patients treated in the UK National Health Service (NHS) BTT program

Methods

Clinical outcomes

There are 6 designated centers responsible for undertaking LVAD implantation and HT in the UK. Data are collected from individuals eligible for HT who enter the program and are held and maintained in the UK Blood and Transplant Data Base (BTDB), an administrative registry. We included all patients who received an HW or HM II as a BTT, bridge to decision for HT, or bridge to myocardial recovery between May 2002 and December 2011. Of 235 patients in the database who received second- or third-generation devices, 125 received the HW and 82 the HM II. The main demographic characteristics of these patients are summarized in Table 1. Two centers implanted 83% of HM II and 86% of HW devices. Before 2007, 5% of the HM II devices were implanted, and before 2009, only 4% of HW. Most (84%) HW devices were implanted from 2010 to 2011, whereas HM II use has been more extended: 36% from 2010 to 2011, 37% from 2008 to 2009, and 27% pre-2008. These data imply a faster learning curve for HW surgery, and that with time in the UK program, the proportion of HW implants has grown relative to that of HM II.

Table 1 Demographic Characteristics of Blood and Transplant Data Base Patients who Received HeartMate II or HeartWare Devices[a]

Characteristic[b]	HM II ($n = 82$)	HW ($n = 125$)
Age, y		
Mean (SD)	40.8 (14.4)	47.7 (12.0)
Median (range)	43 (16-66)	49.5 (17-66)
Gender		
Male	64/78 (82.1)	113/125 (90.4)
Female	14/78 (17.9)	12/125 (9.6)
Ethnicity		
White	64/78 (84.3)	113/125 (90.4)
Asian/Asian-British	5/78 (6.8)	6/125 (4.8)
Black/Black-British	6/78 (7.9)	4/125 (3.2)
Other	1/78 (1.3)	2/125 (1.6)
Height, mean (SD) cm		
Male	175.9 (8.6)	177.3 (7.3)
Female	162.4 (8.6)	163.5 (5.2)
Weight, mean (SD), kg		
Male	78.1 (13.3)	83.8 (16.4)
Female	65.6 (13.4)	63.4 (9.3)
Systolic BP, mean (SD) mm Hg	97.1 (12.1)	98.1 (4.1)
Medication use[c]		
ACE inhibitor	19/64 (29.7)	67/123 (54.5)
Angiotensin receptor blocker	6/62 (9.7)	17/122 (13.9)
β-Blocker	28/66 (42.4)	75/119 (63.0)
Inotrope use	56/71 (78.9)	86/122 (70.5)
Diabetic	5/76 (6.6)	25/124 (20.2)
Smoking		
Current smoker	9/63 (14.3)	10/110 (9.1)
Former smoker	14/63 (22.2)	39/110 (34.5)
Hypertension	1/67 (1.5)	20/111 (18.0)
Concomitant surgery	6/79 (7.6)	13/125 (10.4)

ACE, angiotensin-converting enzyme; BP, blood pressure; HM II, HeartMate II; HW, HeartWare; SD, standard deviation.

[a]Database entries recorded as unknown or missing were few and were excluded from the calculations. There were more missing and unknown entries for HeartMate II (Thoratec, Pleasanton, CA) than for HeartWare (HeartWare International, Framingtom, MA).

[b]Categoric variables are shown as number (%) and continuous variables as indicated.

[c]Depending on how data were accrued patients may have discontinued -blockers before receiving ACE inhibitors or some received both treatments.

Principal outcomes recorded in the BTDB after implantation of an LVAD were HT, explantation of the device, continuation alive with the originally implanted device, and death while supported with the originally implanted device. We investigated outcomes with Kaplan-Meier (KM) time-to-event analyses and with cumulative incidence methodology for competing outcomes.[16] Statistical analyses were conducted in Stata SE 11 software (StataCorp LP, College Station, TX).

Economic model and model inputs

We adopted a previously developed model[17] to assess the cost-effectiveness of the UK BTT program (Figure 1). The model has a

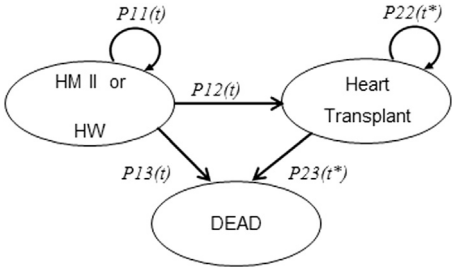

Figure 1 Semi-Markov discrete-time multistate model for Heart Mate II (Thoratec, Pleasanton, CA) and HeartWare (HeartWare International, Framingham, MA) patients: *P11*(*t*), probability of a ventricular assist device (VAD) patient surviving *t* months after VAD implant; *P12*(*t*), probability a VAD patient receives a heart transplant *t* months after VAD implant; *P13(t)*, probability of a VAD patient dying *t* months after VAD implant, before heart transplantation; *P22(t*)*, probability of a transplant recipient surviving *t** months after heart transplantation; *P23(t*)*, probability of a transplant recipient dying *t** months after heart transplantation.

semi-Markov multistate structure and was built using Excel software (Microsoft, Redmond, WA). Each patient in the model exists in 1 of 3 mutually exclusive health states: state 1, alive on LVAD; state 2, alive after HT; state 3, dead (the absorbing health state). The monthly transition probabilities between health states are represented by the quantities *p12, p13,* and *p23.* Transition between states occurs at the end of each cycle, and cycle length was 1 month. We estimated transition probabilities for death amongst those who received an with a LVAD (*p13*) or with HT (*p23*), and time to HT (*p12*) using individual patient data (IPD) KM time-to-event analyses for recipients of HM II, HW, and HT. We used parametric extrapolation beyond observed data as necessary.

KM time-to-death plots (*p13* and *p23*) were strongly biphasic. Poor initial survival was followed by improved survival with a fairly constant hazard. However, when smaller proportions (<10%) remained at risk, KM curves were associated with uncertainty. Therefore, constant hazards were fitted to the first phase of the KM plots (2 months for survival on LVAD support and 3 months for post-HT survival), and then to the second phase until 10% of patients remained at risk (20 for HW and 34 months for HM II), and to 20% remaining at risk after HT (7 years). These second constant hazards were used for extrapolation beyond the observed data.

For survival post-HT, an adjustment was made so that modelled probability of survival never exceeded the age- and gender-matched UK population. Survival post-HT was based on IPD for the 1,101 HT recipients in the BTDB. We applied the same probability of receiving a donor heart (*p12*) to all patients, which was estimated from the IPD time to transplant for all 235 patients. We used an exponential fit to the data as the best parametric distribution amongst exponential, lognormal, loglogistic, Weibull, and Gompertz, according to Akaike's information criterion (AIC). Expert clinical opinion indicated that the probability of receiving a donor heart beyond 3.5 years was extremely low; we therefore set *p12* to be 0 after 42 months. In sensitivity analysis, we used post-HT survival reported by Russo et al[18] in 2009.

In accordance with current UK guidelines, health outcomes were measured in quality-adjusted life years (QALYs).[19] We used the New York Heart Association (NYHA) classification of patients in the BTBD to determine EQ-5D utility scores.[20] For those who received an LVAD, NYHA class was recorded at initial registration and at the 1-month follow-up. For HT recipients, NYHA class recorded at 3-, 12-, and 24-month assessments was used. Health state utilities were assumed to remain constant after implantation with an LVAD[21] and after HT.[22]

Cost inputs were based on a previous analysis[5] and inflated to current prices by applying the projected health services cost index.[23] We obtained costs of LVAD devices from the 6 designated UK centers and calculated a weighted average according to the LVAD throughput at each center. Mean cost for the HW was £80,076 ($127,104) and ranged from £76,774 to £98,160 ($121,863–$155,809); the mean cost for the HM II was £89,830 ($142,587) and ranged from £78,877 to £126,702 ($125,201–$201,113). We estimated LVAD implant procedure cost based on information from 1 center. We used cost of the implant procedure reported by Moreno et al[24] in 2012 in the sensitivity analysis.

Probabilistic sensitivity analysis was undertaken to account for uncertainty in individual patient outcomes and uncertainty in parameters. The beta distribution was used for transition probabilities and utilities, and the gamma distribution was used for costs.[25] Univariate sensitivity analysis was used to investigate the effect of increasing and decreasing base case input variable values by 30%. All model inputs are summarized in Table 2.

The model was run for a lifetime horizon (50 years), and shorter time horizons of 3 and 10 years were explored in sensitivity analyses. We evaluated costs and benefits from the perspective of the UK NHS (that is, only activities undertaken within the NHS and costs met by the NHS were considered). An annual discount rate of 3.5% was applied to costs and benefits[19]; all costs are reported in 2011 GB£. Model outputs include mean life-years gained (LYG), mean QALYs, mean costs, and mean incremental cost-effectiveness ratios (ICERs), calculated as £/LYG and £/QALY gained.

Results

Clinical outcomes

Figure 2 summarizes the cumulative incidence of competing outcomes for HM II and HW recipients. Follow-up was more extended for HM II patients than for HW patients. According to the competing-outcome analysis, the estimated proportion of patients who died on LVAD support at 12 months was 20.5% for HW and 24% for HM II patients, and by 24 months, the proportions were 22% for HW and 31.5% for HM II. At 750 days, irrespective of LVAD device, only about 11% of patients had undergone successful transplantation with a donor heart. This low rate of HT extended to the end of follow-up for both sets of patients and presumably reflects the low availability of donor hearts within the UK.[2] A greater proportion of patients were alive with HW support at 750 days (63%) than with HM II support (~40%).

Figure 3 summarizes KM time-to-event analyses for survival on LVAD support, for survival after HT, for time to HT, and also the parametric modelling to the observed data. Observed and modelled survival was superior for the HW recipients. According to KM analysis at 6 months, there was little difference in survival between groups. By 12 months, an estimated 24% of HW patients and 34% of HM II recipients had died.

Table 3 summarizes base case deterministic and probabilistic results in mean costs accrued, mean life-years

Table 2 Summary of the Base Case Deterministic and Probabilistic Model Inputs

			Beta distribution	
Health state transition probabilities (*p*)[a]	Mean	SE	Alpha	Beta
HW VAD support to death *p13*				
Month 1-2	0.055879442	0.0317	2.86	48.4
Month ≥3	0.014119275	N/A	N/A	N/A
HM II VAD support to death *p13*				
Month 1-2	0.063555656	0.0398	2.31	34.17
Month ≥3	0.023391965	N/A	N/A	N/A
Time to HT *p12* HW and HM II				
Month 1-42	0.012745641	N/A	N/A	N/A
Month ≥42	0			
Support on HT to death *p23* HW & HM II				
Month 1–3	0.070366726	0.0163	17.2	227.25
Month 4–284	0.002980948	N/A	N/A	N/A
Month ≥284	As UK pop'n	N/A	N/A	N/A
Health state utility				
Post-HW VAD all months	0.75	0.006	2,869.14	949.35
Post-HM II VAD all months	0.73	0.008	1,976.61	745.84
Post HT all months	0.83	0.005	4,683.69	959.31
Cost item (£)			Gamma distribution	
			Alpha	Beta
HW VAD device	80,076	N/A	N/A	N/A
HM II VAD device	89,830	N/A	N/A	N/A
VAD implant procedure	3,728	N/A	N/A	N/A
Post-VAD implant support				
HW Month 1[b]	109,581	3996	751.68	145.78
HM II Month 1[b]	119,336	4367	746.44	159.87
HW & HM II				
Month 2	13,440	1306	105.95	126.84
Month 3	5,110	764	44.69	114.32
Month 4	3,836	607	40	95.89
Month 5	3,248	460	49.89	65.09
Month 6	2,326	356	42.69	54.48
Month ≥7	1,893	907	4.35	434.97
HT theater cost HW & HM II	16,663	N/A	N/A	N/A
Post-HT costs HW & HM II				
Month 1	2,240	1117	832.97	38.7
Month 2	4,331	802	29.18	148.4
Month 3	2,609	470	30.77	84.79
Month 4	2,828	260	117.87	23.99
Month 5	2,179	432	25.42	85.7
Month 6	1,646	138	142.69	11.53
Month ≥7	1,410	1,780	62.91	22.41

HM II, HeartMate II (Thoratec, Pleasanton, CA); HT, heart transplant; HW, HeartWare (HeartWare International, Framingham, MA); N/A, not applicable; SE, standard error; UK pop'n, United Kingdom population; VAD, ventricular assist device.

[a] *p12* , *p13*,and *p23* refer to transition probabilities shown in Figure 1.

[b] Includes device and procedure.

gained (LYG), and mean QALYs in each treatment group for the lifetime horizon of 50 years. The probabilistic analysis found individuals who received the third-generation HW incurred more costs but accrued more life-years and QALYs than did HM II recipients. The base case probabilistic analysis indicates that implanting the third-generation HW compared with implanting the second-generation HM II would cost the NHS an average of an additional £24,379 ($38,697) over the lifetime of an individual (95% confidence interval, –£46,527 to £108,940 [–$73,852 to $172,920]), with an ICER of £20,799 ($33,014)/QALY gained (95% confidence interval, dominant to £79,837 [$126,725]). The deterministic ICER was slightly higher. The main reason for the greater expense of the HW option is that more patients survive to HT, which incurs greater costs (e.g., for HT surgery and after care).

Figure 4 illustrates probabilistic results for 3-year, 10-year, and lifetime horizons distributed on the cost-effectiveness

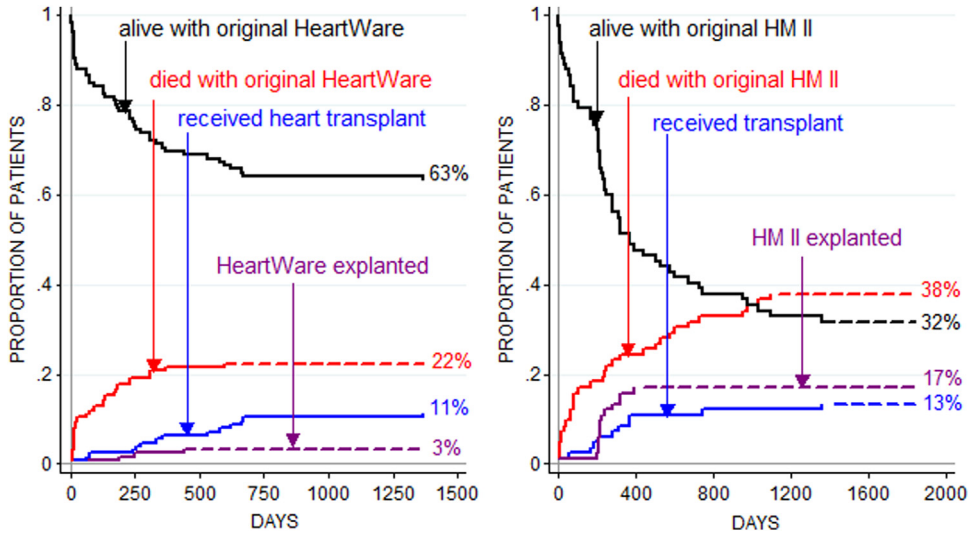

Figure 2 Competing outcomes analysis for (left) HeartWare (HW; HeartWare International, Framingham, MA) and (right) Heart Mate II (HM II; Thoratec, Pleasanton, CA) patients. Outcomes were died while being supported by the original ventricular assist device (VAD), received a heart transplant, or the VAD removal.

plane. Each data point represents one of the model's 1,000 iterations. The slope of the line indicates the mean incremental cost-effectiveness of the intervention. Figure 4 also shows the cost-effectiveness acceptability curves (CEACs) for the 3 time horizons. The CEAC highlights that at a willingness-to-pay threshold of £20,000 ($31,476)/QALY, the probability that implanting the HW is cost-effective is 0.51, 0.51, and 0.50 over the 3-year, 10-year, and lifetime time horizons, respectively.

Sensitivity analysis

Sensitivity analysis shows that either changing modelled survival probability after transplant (*p23*), in line with data reported by Russo et al[18] (Figure 3; Table 3) or changing the cost of the implant procedure in line with Moreno et al[24] had little effect on the ICER. Figure 5 highlights that the deterministic lifetime ICER is relatively

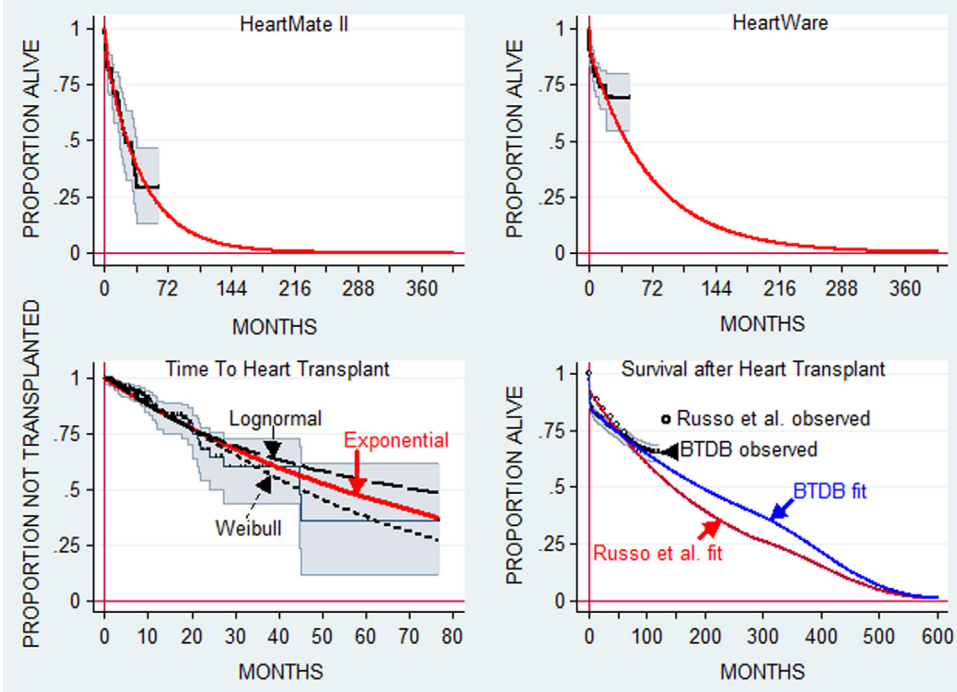

Figure 3 Time-to-event analyses and modelling of individual patient data in the United Kingdom National Health Service Blood and Transplant Data Base (BTDB). Kaplan-Meier plots (shaded area shows 95% confidence interval) of survival while supported with (left) Heart Mate II (HM II; Thoratec, Pleasanton, CA), (right) Heart Ware (HW; HeartWare International, Framingham, MA), or with a heart transplant, and time to heart transplant. The continuous lines represent modelled curves. Patients supported with a ventricular assist device (VAD) were censored if alive at the end of follow-up, at time of removal of a VAD, and at time of receipt of a transplant. For time-to-transplant analysis patients, were censored on death and at time alive at end of follow-up if they had not received a donor heart. Heart transplant patients were censored if alive at the end of follow-up.

Table 3 Summary of Base Case and Sensitivity Analysis Results

	Deterministic analysis lifetime model		
Variable	Mean cost UK, £	Mean survival, y	Mean QALYs
HW VAD	258,913	6.30	4.99
HM II VAD	231,871	4.87	3.84
Difference	27,042	1.42	1.14
ICER (£/LYG)	18,978		
ICER (£/QALY)	23,530		
	Probabilistic analysis lifetime model		
	Mean cost UK £	Mean survival, y	Mean QALYs
	(95% CI)	(95% CI)	(95% CI)
HW VAD	256,867 (206,110 to 332,598)	6.34 (5.26 to 7.48)	5.02 (4.14 to 5.99)
HM II VAD	232,488 (189,487 to 286,308)	4.90 (3.75 to 6.01)	3.85 (2.99 to 4.78)
Difference	24,379 (−46,527 to 108,940)	1.43 (0.42 to 2.57)	1.17 (0.36 to 2.06)
ICER, £/LYG	16,978 (dominates to 86,586)		
ICER, £/QALY	20,799 (dominates to 79,837)		
	Univariate sensitivity analyses		
	ICER £/QALY	Difference in QALYs	Difference in costs (£)
Post-HT survival as Russo[a] (*p23*)[b]	23,576	1.14	26,916
Implant cost as Moreno[a]	24,058	1.14	27,649
3-year time horizon	12,969	0.22	2,955
10-year time horizon	22,954	0.75	17,429

CI, confidence interval; HM II, HeartMate II (Thoratec, Pleasanton, CA); HT, heart transplant; HW, HeartWare (HeartWare International, Framingtom, MA); ICER, incremental cost effectiveness ratio; LYG, life-years gained; QALY, quality-adjusted life-year; VAD, ventricular assist device.

[a]Lifetime horizon.

[b]*p23* refers to the transition probability shown in Figure 1.

robust to increasing and decreasing important base case inputs by 30%.

Discussion

The shortage of donor hearts means that LVADs will often be the only treatment option available for this ever-expanding patient population. However, the increasing range of LVADs necessitates a closer look at their relative effectiveness and cost-effectiveness. We used individual patient data from the UK NHS BTDB to investigate the relative costs and consequences of implanting individuals with the 2 most commonly used LVADs. We found that HW was associated with an ICER of £20,799 ($33,014)/QALY compared with the older second-generation HM II. Over a 3-year time horizon, the ICER reduces to about £12,000 ($19,048)/QALY.

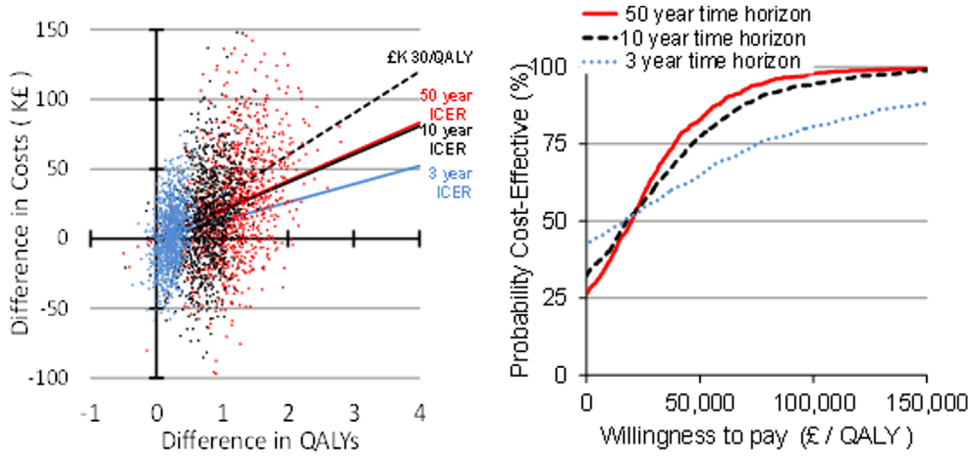

Figure 4 Incremental cost-effectiveness ratios (ICERs) and cost-effectiveness acceptability curves are shown for 3-year, 10-year, and lifetime horizons for the comparison of Heart Ware (HeartWare International, Framingham, MA) vs Heart Mate II (Thoratec, Pleasanton, CA) ventricular assist devices. QALY, quality-adjusted life-years.

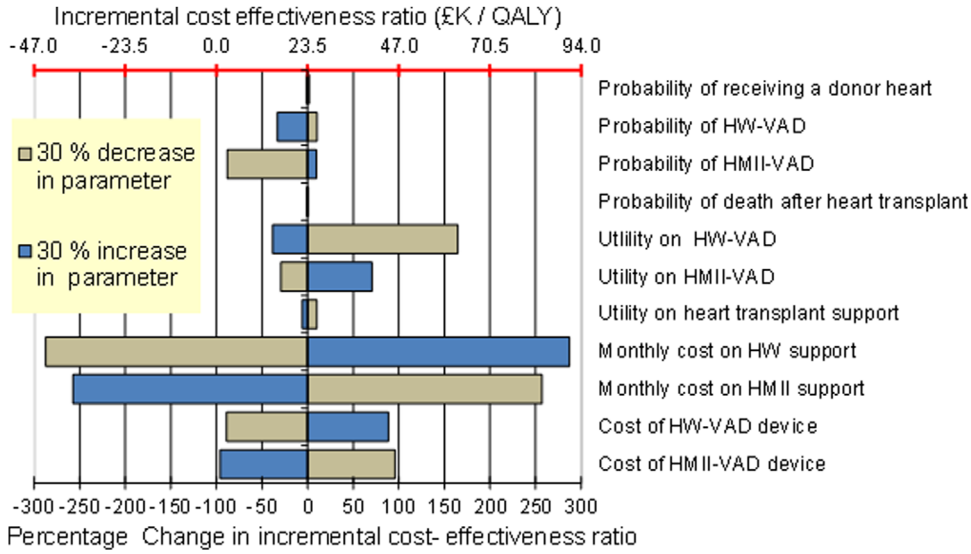

Figure 5 Tornado diagram depicts the results from sensitivity analyses in which the named model input parameters were increased and decreased by 30%. Negative incremental cost-effectiveness ratios show that the HeartWare (HW; HeartWare International, Framingham, MA) ventricular assist device (VAD) dominates the Heart Mate II (HM II; Thoratec, Pleasanton, CA), indicating it is more effective and less costly. QALY, quality-adjusted life years.

Until recently, there have been concerns that the smaller third-generation LVADs may not perform as well as the larger second-generation LVADs.[26] The KM plots (Figure 3) indicate superior survival for HW relative to HM II recipients in the immediate post-operative months and in the long-term. Although there may be little reason to suspect that choice of device depends on patient characteristics, the lack of random allocation means the comparison is at risk of bias. Survival for recipients of the HW has been reported for 2 multicenter trials of 50 and 140 patients.[4,27,28] These reported 1-year survivals of 85% and 86%, respectively, and a 2-year survival of 79%.[4] In the HM II United States (US) Food and Drug Administration-approval trial of 133 patients (ClinicalTrials.gov number, NCT00121472), survival at 1 year was 68%.[29] In extensions of this trial, a 1-year survival of 73% was reported for 281 patients[30] and of 75.6% for 486 patients.[31] Overall, these data support improved survival for patients receiving the HW vs the HM II. Retrospective analysis also revealed improved 1-year survival for the latter groups of 73% and 84.9%.[31]

The competing outcomes analysis indicated that a relatively low proportion of patients in the UK BTT program proceed to successful HT (~11% after 750 days). This result is quite different from that seen from competing outcome analyses in the international literature. In the US multicenter HM II study of 281 patients, 56% received HT by 18 months.[30] Similarly in the smaller multicenter European study of 50 patients with the HW, 40% received HT by 2 years.[4] The most recent published study of the HW device (140 patients)[27] reported that approximately 29% received a HT by 6 months and 40% by 1 year. John et al[31] compared the 48% receiving HT within the US multicenter HM II trial ($n = 486$) with the 39% who received HT in the post-trial era subsequent to US FDA approval. All of these studies report much higher rates for HT than observed for the UK program, presumably reflecting a lower availability of donor organs.

A weakness of this study (as with all studies of these devices) is the lack of a randomized comparison between different devices. There are several candidate explanations for the differences seen in device performance; for example, the HW device avoids abdominal surgery, populations and practices may change with time, and 84% of HW devices were implanted from 2010 to 2011 whereas HM II use has been more extended at 36% from 2010 to 2011, 37% from 2008 to 2009, and 27% pre-2008. In the absence of randomized evidence, a potential strength of our analysis is the use of the BTDB IPD for the derivation of transition probabilities between health states and of utilities. However, that time-to-event analyses are not free of bias is possible. In addition, extrapolation beyond the observed data was required to model survival, and this inevitably leads to uncertainty regarding the estimation of transition probabilities in the longer term. Although the use of simple constant hazard models may be problematic, others have adopted similar procedures.[17,24]

Economic modelling required a number of assumptions that were effectively investigated in sensitivity analyses. A disadvantage is that because the BTDB did not collect direct health-related quality of life measures, we had to use a published algorithm to derive utilities for the different health states.[20] This will continue to hamper economic evaluations of LVADs in the UK until these data can be routinely collected as part of the BTDB. Furthermore, bottom-up analysis of the current costs associated with maintenance on LVAD support is required.

Although our analysis shows that the HW may be a preferred device to the HM II, unhesitatingly recommending HW over HM II remains difficult owing to the lack of head-to-head randomized comparisons of the clinical effectiveness of the devices. The prospect of abdominal surgery required for the HM II might possibly deter intervention for some patients who might be considered candidates for the

HW device. The differences between the 2 patient groups, as summarized in Table 1, also potentially suggest the possibility of individualized or personalized treatment which, in turn, means cost-effectiveness results should not necessarily favor one device over the other. Nevertheless our findings may aid clinicians and decision makers when they consider the use of different LVADs, especially within the NHS- supported BTT program.

In summary, we conclude from our economic evaluation that within the UK NHS BTT program, the HW device yields greater benefit than the HM II at an extra lifetime cost of approximately £23,530/QALY. The extra cost derives from better survival with the HW device, and this translates to a greater proportion receiving a HT with its associated short-term and long-term costs.

Disclosure statement

This work was supported by the National Institute for Health Research Health Technology Assessment Programme, UK. Project number 12/02/01

The authors acknowledge the following for their advice and expert contributions:

Dr Mark Petrie, Consultant Cardiologist Golden Jubilee National Hospital, Glasgow, and Director of the Scottish National Advanced Heart Failure Service; Dr Jayan Parameshwar, Consultant Cardiologist, Transplant Physician, and Steven Tsui, Clinical Director of Transplant Services, Papworth Hospital NHS Foundations Trust; Dr Guy MacGowan, Consultant Cardiologist, Freeman Hospital, and Professor Stephan Schueler, Consultant Cardiac Surgeon, The Newcastle Upon Tyne Hospitals; Saleem Haj-Yahia, Consultant Transplant Surgeon and Deputy Director of the Scottish National Advanced Heart Failure Service; Professor John Wallwork, retired transplant surgeon; Professor Martin Buxton, Professor of Health Economics, Health Economics Research Group, Brunel University; Dr Linda Sharples, Programme Leader, MRC Biostatistics Unit, Institute of Public Health, University of Cambridge; Dr Ewen Cummings, McMDC Consulting, Glasgow; and Duncan Ambrose, Senior Commissioning Manager at NHS National Specialised Commissioning Team. The authors are extremely grateful to NHS Blood and Transplant staff for continuing advice and support, including advice on the BTDB, and to Dr S Moreno (Fundacio Clinic, Barcelona) for constructive discussion of the economic model and generous sharing of data. Professor Aileen Clarke is also supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care West Midlands at University Hospitals Birmingham NHS Foundation Trust. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

The views expressed in this report are those of the authors and not necessarily those of the National Institute for Health Research Health Technology Assessment Programme. Any errors are the responsibility of the authors.

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

References

1. British Heart Foundation Health Promotion Research Group. Coronary heart disease statistics: 2010 edition. Available from: http://www.bhf.org.uk/research/statistics.aspx. Accessed May 24, 2013.
2. Connolly M, Beattie J, Walker D. End of life care in heart failure; a framework for implementation. Available from: http://webarchive.nationalarchives.gov.uk/20130718121128/http://www.endoflifecare.nhs.uk/download.ashx?mid=3041&nid=3043. Accessed January 24, 2014.
3. Clegg AJ, Scott DA, Loveman E, et al. The clinical and cost-effectiveness of left ventricular assist devices for end-stage heart failure: a systematic review and economic evaluation. Health Technol Assess 2005;9:1-132.
4. Strueber M, O'Driscoll G, Jansz P, et al. Multicenter evaluation of an intrapericardial left ventricular assist system. J Am Coll Cardiol 2011;57:1375-82.
5. Sharples LD, Buxton M, Caine N, et al. Evaluation of the ventricular assist device programme in the UK. Health Technol Assess 2006;10:iii-108.
6. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 2009;361:2241-51.
7. Birks EJ. Left ventricular assist devices. Heart 2010;96:63-71.
8. Nguyen DQ, Thourani VH. Third-generation continuous flow left ventricular assist devices. Innov Technol Tech Cardiothorac Vasc Surg 2010;5:250-8.
9. Krishnamani R, DeNofrio D, Konstam MA. Emerging ventricular assist devices for long-term cardiac support. Nat Rev Cardiol 2010;7:71-6.
10. Timms D. A review of clinical ventricular assist devices. Med Eng Phys 2011;33:1041-7.
11. Drews T, Stepanenko A, Dandel M, Buz S, Lehmkuhl HB, Hetzer R. Mechanical circulatory support in patients of advanced age. Eur J Heart Fail 2010;12:990-4.
12. Klotz S, Stypmann J, Welp H, et al. Does continuous flow left ventricular assist device technology have a positive impact on outcome pretransplant and posttransplant? Ann Thorac Surg 2006;82:1774-8.
13. Oswald H, Schultz-Wildelau C, Gardiwal A, et al. Implantable defibrillator therapy for ventricular tachyarrhythmia in left ventricular assist device patients. Eur J Heart Fail 2010;12:593-9.
14. Sandner SE, Zimpfer D, Zrunek P, et al. Renal function and outcome after continuous flow left ventricular assist device implantation. Ann Thorac Surg 2009;87:1072-8.
15. Sandner SE, Zimpfer D, Zrunek P, et al. Age and outcome after continuous-flow left ventricular assist device implantation as bridge to transplantation. J Heart Lung Transplant 2009;28:367-72.
16. Coviello V, Boggess M. Cumulative incidence estimation in the presence of competing risks. Stata J 2004;4:103-12.
17. Sharples LD, Dyer M, Cafferty F, et al. Cost-effectiveness of ventricular assist device use in the United Kingdom: results from the evaluation of ventricular assist device programme in the UK (EVAD-UK). J Heart Lung Transplant 2006;25:1336-43.
18. Russo MJ, Hong KN, Davies RR, et al. Posttransplant survival is not diminished in heart transplant recipients bridged with implantable left ventricular assist devices. J Thorac Cardiovasc Surg 2009;138:1425-32.
19. National Institute for Health and Clinical Excellence. Guide to the methods of technology appraisal. Available from: http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf. Accessed May 29, 2012.
20. Gohler A, Geisler BP, Manne JM, et al. Utility estimates for decision-analytic modeling in chronic heart failure—health states based on New York Heart Association classes and number of rehospitalizations. Value Health 2009;12:185-7.
21. Rogers JG, Bostic RR, Tong KB, Adamson R, Russo M, Slaughter MS. Cost-effectiveness analysis of continuous-flow left ventricular assist devices as destination therapy. Circ Heart Fail 2012;5:10-6.
22. Aaronson KD, Patel H, Pagani FD. Patient selection for left ventricular assist device therapy. Ann Thorac Surg 2003;75(6 Suppl):S29-35.
23. Curtis L. Personal Social Services Research Unit. Unit costs of health and social care, 2010. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/182162/PSSRU-1368-230X.pdf. Accessed: June 18, 2012.
24. Moreno SG, Novielli N, Cooper NJ. Cost-effectiveness of the implantable HeartMate II left ventricular assist device for patients

awaiting heart transplantation. J Heart Lung Transplant 2012;31:450-8.
25. Briggs A, Sculpher M, Claxton K. Decision modelling for health economic modelling. 1 ed.Oxford University Press; 2006.
26. Hosseini MT, Popov AF, Simon AR, Amrani M, Bahrami T. Comparison of left ventricular geometry after HeartMate II and HeartWare left ventricular assist device implantation. J Cardiothorac Surg 2013;8:31.
27. Aaronson KD, Slaughter MS, Miller LW, et al. Use of an intrapericardial, continuous flow, centrifugal pump in patients awaiting heart transplantation. Circulation 2012;125:3191-200.
28. Strueber M, Sander K, Lahpor J, et al. HeartMate II left ventricular assist device; early European experience. Eur J Cardiothorac Surg 2008;34:289-94.
29. Miller LW, Pagani FD, Russell SD, et al. Use of a continuous-flow device in patients awaiting heart transplantation. [Reprint in Nat Clin Pract Cardiovasc Med 2008;5:80–1]. New Engl J Med 2007;357:885-96.
30. Pagani FD, Miller LW, Russell SD, et al. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol 2009;54:312-21.
31. John R, Naka Y, Smedira NG, et al. Continuous flow left ventricular assist device outcomes in commercial use compared with the prior clinical trial. Ann Thorac Surg 2011;92:1406-13.